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## Optimization of correction of sleep, speech and cognitive disorders in children due to perinatal CNS injury

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The article shows the results of a clinical study on the effectiveness and tolerability of the use of the food supplement "Anantavati® Kids" (by Ananta Medicare) in children with speech and cognitive disorders and sleep disorders due to perinatal injury of the central nervous system. The specifics of the effect of Bacopa Monnieri and Withania somnifera on the functional changes of the brain in the main group of children receiving Anantavati® Kids and the comparison group are shown. During the clinical observation of the use of the phytocomplex Anantavati® Kids (a fixed combination of Bacopa Monnieri – 150 mg and Withania somnifera – 300 mg), 38 children aged 4 to 12 years, who received "Anantavati® Kids" in addition to rehabilitation psychological and speech therapy measures, were examined. For comparison, 20 children who had similar syndromes and received only rehabilitative psychological and speech therapy measures were examined. The groups were comparable in terms of gender and age. The effectiveness, tolerability, and safety of the food supplement "Anantavati® Kids" in behavioural disorders, speech, cognitive and sleep disorders due to perinatal injury of the central nervous system in children were evaluated by using neurophysiological methods, neuropsychological indicators, and statistical methods.

The children of the first group received "Anantavati® Kids" syrup for 30 days, while undergoing two clinical-neurological, neuropsychological, speech therapy and neurophysiological examinations: immediately before the start of the course and 1 month after taking "Anantavati® Kids". A positive effect, according to individual assessment of the clinical condition in dynamics after 1 month of use of "Anantavati® Kids", was registered in most children. In the main group, the prevalence of complaints about sleep disorders decreased by 71%, speech disorders – by 47.37%, hyperactivity – by 55.26%, memory disorders – by 42.11%, attention disorders – by 65.79 %, emotional sphere disorders – by 63.16%. Positive dynamics of speech therapy indicators, in the form of an increase and active use of vocabulary, an increase in the compositional structure of words and the volume of coherent speech, were observed in 18 (47.37%) children. After the course of Anantavati® Kids, 28 (73.68%) children of the main group had pronounced positive dynamics of EEG indicators. A good safety profile was noted when using "Anantavati® Kids". This is manifested by good tolerability during the study. Thus, the analysis of the data obtained after the use of Anantavati® Kids in children with the consequences of perinatal injury of the central nervous system demonstrates the profound effect of Anantavati® Kids on sleep disorders, symptoms of cognitive and speech and psychoemotional disorders against the background of course admission.

**Keywords:** cognitive disorders, speech disorders, sleep disorders, behavioural disorders, food supplement "Anantavati® Kids".

The problem of perinatal pathology, including the central nervous system (CNS), remains one of the urgent medical issues for a long time. According to the State Statistics Committee of Ukraine, conditions arising in the perinatal period, make 18% and take a second place in the morbidity structure of children under 1.5 years of age [1]. Signs of damage to the central nervous system are registered in 65-75% of children in the neonatal period. Neurological pathology occurs in about 30% of children at the age of 1 year. The formation of language, the formation of intelligence, and the development of static-kinetic functions take place in the first years of a child's life. In older children, the incidence of neurological disorders of perinatal genesis is quite high and the indicator is constantly increasing [2].

Therefore, timely diagnosis and treatment of neurological diseases in childhood affect the entire future life of a person, his physical and mental state and social adaptation.

In modern life, there is an increasing influence of social and environmental factors on the development and activity of the child, which, in combination with the increase in the prevalence of perinatal lesions of the central nervous system, are the reasons for the increase in mild forms of cerebral pathology. Cerebral pathology is one of the most common neuropsychological disorders in childhood, and is manifested by age immaturity of certain high mental functions and their disharmonious development. Children with this pathology experience significant difficulties in learning and social adaptation. These disorders are characterized by learning difficulties, inattention, poor logical thinking, memory and attention disorders, and disorders of motor skills such as poor orientation, dysarthria, clumsiness, impulsivity, irritability, hyperactivity, sleep disorders [3].

One of the urgent tasks of children's neurology is the search for effective criteria for early diagnosis and prediction of neuropsychological disorders in different age periods, the development of differentiated rehabilitation programs for children from "risk groups" of children's neurological diseases and treatment protocols.

Phytotherapy is well tolerated and it is successfully used for sleep disorders, increased anxiety and irritability, impulsivity, aggressiveness, hyperactivity, anxiety, mood swings, depression, and social dysfunction. According to sociological studies, plant-based products used for the treatment and prevention of various diseases make about 40%. The population prefers treatment with herbs and traditional remedies of natural origin [4].

In order to correct CNS disorders in children with the consequences of perinatal injury, we considered the possibility of using the herbal complex Anantavati® Kids, which includes extracts of *Withania somnifera* and *Bacopa monnieri*. These phytocomponents have become widespread in world clinical practice and have polymodal pharmacodynamics [5–8].

Due to components, such as cytoindosides VII and VIII, vananolides and steroid lactones (withanone, withaferin), alkaloids (ashwagandolin, isopellethrine, anaferin) *Withania somnifera* exerts anti-stress, antioxidant, neuromodulating effects on GABA and GABAergic neuromodulation and reduces the level of the stress hormone cortisol. Activation of GABAergic processes is necessary to ensure falling asleep and normalization of the physiological structure of sleep [7].

The uniqueness of *Bacopa Monnieri*'s action is due to its composition, which contains saponins (bacosides A and B), alkaloids (brahmin, herpestine), flavonoids (apeginine, luteonine), phytosterols ( $\beta$ -sitosterol, betulinic acid, stigmasterol), sapogenin, and glycosides. First of all, the active components of this extract (in particular, bacosides) have antioxidant and nootropic properties, and contribute to the improvement of neurotransmission and affect the release of neurotransmitters (acetylcholine, dopamine, GABA and serotonin [6,8].

During the clinical study, 38 children aged 4 to 12 years, who had speech disorders, cognitive disorders and sleep disorders due to perinatal damage to the central nervous system, received Anantavati® Kids in addition to rehabilitation psychological and speech therapy measures. 20 boys and 18 girls took part in the study. The average age of children was  $8 \pm 4$  years. (Table 1). For comparison, 20 children of the comparison group were examined. They had similar syndromes and received only rehabilitative psychological and speech therapy measures, comparable in terms of gender and age: 12 boys and 8 girls aged 4-6 years – 9 children, 7-10 years – 7 children, 11-12 years old – 4 children.

The criteria for including patients in the study were as follows:

- informed consent of the patient and his parents to participate in the study,
- consent for participation in research,
- patient age from 4 to 12 years,
- speech disorders, cognitive disorders and sleep disorders due to perinatal CNS injury,
- absence of concomitant somatic diseases in the patient during the study period.

Patients received Anantavati® Kids syrup for 30 days. Dosage regimen: children aged 4–6 years – 5 ml, 7–11 years – 7.5 ml, children aged 12 years – 10 ml, once a day, in the morning after meals.

All patients underwent a two-time clinical-neurological, neuropsychological, speech therapy and neurophysiological examination: immediately before the start of the course and 1 month after taking Anantavati® Kids.

Clinical and neurological examination included the assessment of the general clinical condition and the analysis of neurological status.

The neuropsychological examination included the hearing, visual and kinaesthetic memory tests (according to O. R. Luria). A consultation with a speech therapist and a study of expressive and impressive speech were also carried out.

The neurophysiological examination included recording, quantitative analysis and topographic mapping of electroencephalograms by using a hardware and software complex, which included the DX system electroencephalograph and the BrainTest program.

SPSS Statistics 19.0 and Statistica 64 version 10, Microsoft Excel program for Windows operating system were used for statistical processing of the obtained results.

In the course of statistical processing of the obtained data, the following methods of analysis were used for quantitative signs, the mean error (M), standard error (m), arithmetic mean and standard errors ( $M \pm m$ ) were calculated to detect the reliability of differences – the Student's parametric t-test, obtained the results were considered statistically significant at  $p < 0.05$ .

Among the clinical symptoms in the children of both groups (control and comparison), the following were observed: attention deficit syndrome, hyperactivity syndrome, excessive motor activity inappropriate to the situation, impulsivity, problems in relationships with others, behavioural disorders and learning difficulties, lethargy, drowsiness occurred as a result of movement anxiety, irritability, emotional lability, feeling of fatigue, asthenia causing a pronounced and persistent decrease in mental capacity even with a mild intellectual load, speech and sleep disorders.

According to neuropsychological examinations, impairment of cognitive functions was observed in 26 children (68.42%), impairment of concentration and attention – in 34 children (89.47%), manifestations of impulsive reactions and motor inhibition – in 35 children (92.11%).

According to the data of the speech therapy, 6 children (15.79%) had general speech underdevelopment level II, 11 children (28.95%) – level III, 5 children (13.16%) – level IV.

Before the start of therapy, visual and quantitative analysis of EEG recordings showed that 23 (60.53%) children of the control group had slowing in relation to the age norm (to 5-7 Hz) and hypersynchronization of the occipital  $\alpha$ -rhythm, an increased content of slow-wave activity (Fig. .1), selective absorption of low frequencies (3-8 Hz) of rhythmic photostimulation, which in clinical

electroencephalography is traditionally considered as moderately expressed signs of a reduced functional state of the cerebral cortex.

In 10 (26.32%) children, in the EEG picture, signs of a deficiency of the brain's braking system came to the fore. 9 children (23.68%) had EEG signs of the increased paroxysmal activity in the form of bursts (with an amplitude of up to 150-200  $\mu$ V and more), polymorphic ( $\alpha$ - $\theta$ - $\Delta$ - or peak-wave) discharges (Fig. 2), with amplification or detection (in their absence on the background EEG) during hyperventilation. The normal organized type was registered only in 5 children (13.16%).

In the children of the comparison group, the complaints, neuropsychological data, speech therapy and EEG recordings were almost no different from those of the children in the control group (Table 2).

Assessment of the general clinical condition in dynamics and effectiveness of correction of disorders was carried out individually for each child. At the same time, the criteria for a positive effect were defined as: 1) reduction of subjective complaints and objective symptoms of disorders (in the form of a 25% decrease or more); 2) positive dynamics in neurological status; 3) positive dynamics of EEG data.

According to individual assessment of the clinical condition in dynamics after 1 month of using Anantavati® Kids, a positive effect was registered in most children. In the control group, the prevalence of complaints about sleep disorder decreased by 71%, speech disorder – by 47.37%, hyperactivity – by 55.26%, memory disorder – by 42.11%, attention deficit disorder – by 65.79%, emotional sphere disorders – by 63.16%.

Table 1

**Children divided by age and gender**

Age, years	Number of patients in age groups				Total
	Boys		Girls		
	Absolute value	%	Absolute value	%	Absolute value
4 - 6	9	52.94	8	47.06	17
7 - 10	7	53.85	6	46.15	13
11 -12	4	50	4	50	8
Total	20	52.63	18	47.37	38

Table 2

**The prevalence of clinical syndromes before and after the use of Anantavati® Kids phytocomplex in the control and the comparison groups in children with perinatal CNS injury**

Symptoms	Control group (n = 38)				Comparison group (n = 20)				p	p
	Before using Anantavati® Kids		After using Anantavati® Kids		Basic data		After 1 month of treatment			
	abs.	%	abs.	%	abs.	%	abs.	%		
Sleep disorder	32	84,21	5	13,16	17	85	14	70	p<0,05	p<0,05
Speech disorder	22	57,89	4	10,53	11	55	5	25	p<0,05	p<0,05
Hyperactivity	35	92,11	14	36,84	18	90	15	75	p<0,05	p<0,05
Memory impairment	26	68,42	10	26,32	15	75	13	65	p<0,05	p<0,05
Attention deficit disorder	34	89,47	9	23,68	17	85	13	65	p<0,05	p<0,05
Emotional sphere disorder	35	92,11	11	28,95	18	90	15	75	p<0,05	p<0,05

Table 3

**Characteristics of EEG indicators before and after the use of Anantavati® Kids phytocomplex in the control and the comparison groups in children with perinatal CNS injury**

EEG patterns	Control group (n = 38)				Comparison group (n = 20)				p	p
	Before using Anantavati® Kids		After using Anantavati® Kids		Basic data		After 1 month of treatment			
	abs.	%	abs.	%	abs.	%	abs.	%		
Slowing background activity	23	60,53	5	13,16	12	60	11	55	p<0,05	p<0,05
Paroxysmal activity (bursts of sharp waves)	9	23,68	3	7,89	5	25	4	20	p<0,05	p<0,05
Accelerated $\alpha$ -rhythm	7	18,42	2	5,26	3	15	3	15	p<0,05	p<0,05

According to the results of a neuropsychological examination, after using Anantavati® Kids for 1 month, the cognitive and memory functions improved in 16 (42.11%) children, 25 (65.79%) children became more concentrated and attentive, impulsive reactions and motor inhibition decreased in 21 (55.26%) children, and the emotional sphere stabilized in 24 children (63.16%).

Positive dynamics of logopedic indicators, in the form of an increase and active use of vocabulary, an increase in the compositional structure of words and the volume of coherent speech, were observed in 18 (47.37%) children. The pronunciation of sounds became better in 10 children (55.55%), simple and complex forms of phonemic synthesis and analysis became more accessible in 8 children (44.44%).

After the end of the course of using Anantavati® Kids, 28 children (73.68%) of the control group had pronounced positive dynamics of EEG indicators, which indicates an improvement in the functional state of the brain.

It was manifested in the form of the appearance of occipital  $\alpha$ -rhythm (if it was absent at the beginning of the study) or an increase in its amplitude,  $\alpha$ -index and spectral power (in other types of EEG), and in the normalization of its frequency (in EEG variants with initially slowed or accelerated  $\alpha$ -rhythm) (Fig. 3). In addition, there was a decrease in the severity and spectral power of slow-wave EEG activity in Fig. 1, 2 (including in the EEG reaction to hyperventilation), and a decrease in paroxysmal epileptiform discharges (if available during the first EEG examination) by 15.79% (Table 3, Fig. 4).

When comparing the results of the conducted research, it was found that the children of the control group receiving Anantavati® Kids had significantly ( $p < 0.05$ ) pronounced positive dynamics of clinical syndromes and EEG data than the children of the comparison group (tables 2, 3).

Undesirable effects or allergic reactions were not detected in any of the patients during the observation period. The complex has shown a good tolerability

Figure 1

Patient M., 10 years old. Hypersynchronization of the occipital  $\alpha$ -rhythm, increased content of slow-wave activity before use.

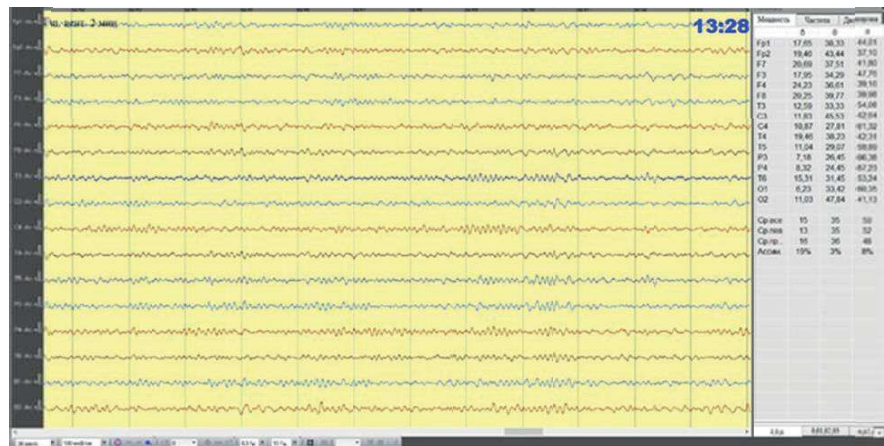


Figure 2

Patient S., 4 years old. EEG signs of the increased paroxysmal activity in the form of bursts of polymorphic  $\theta$ - and  $\Delta$ -discharges before use.

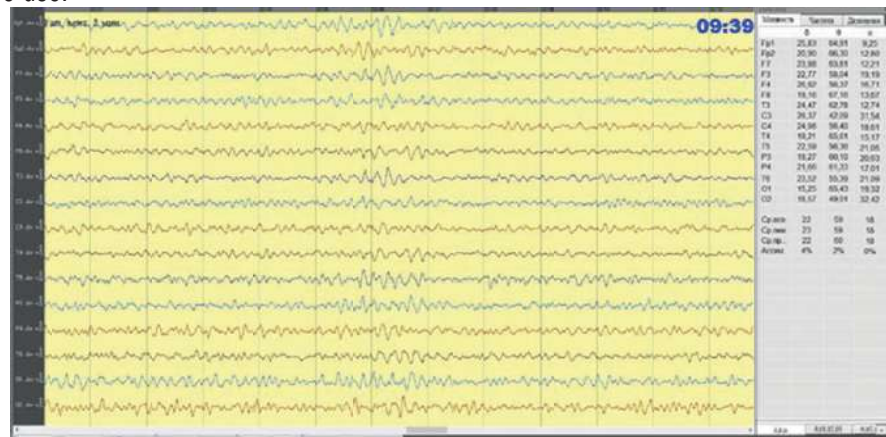


Figure 3

Patient M., 10 years old. Normalization of  $\alpha$ -index and spectral power after a course of use.

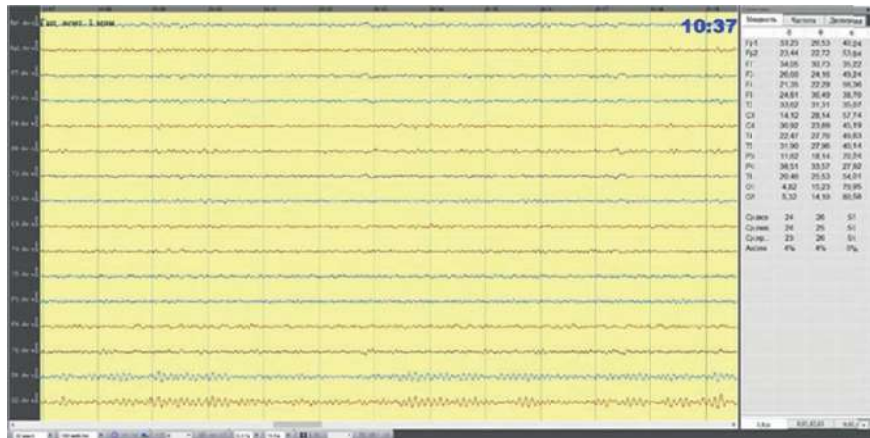
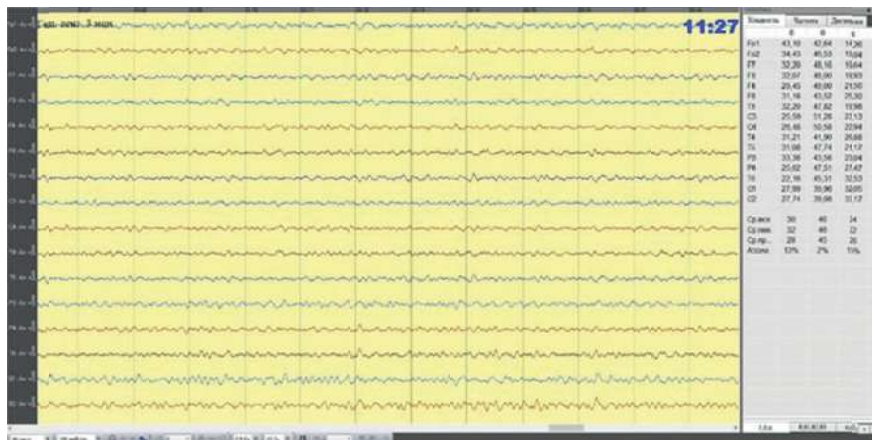


Figure 4

Patient S., 4 years old. Disappearance of paroxysmal discharges after a course of use.



The 1 month use of herbal syrup Anantavati® Kids in children aged 4 to 12 years with speech and cognitive disorders due to perinatal CNS injury allows to:

- improve the functional state of the brain, which is manifested in the improvement of both well-being, clinical and psychometric assessments, and EEG indicators;
- effectively reduce children's complaints about sleep, memory and attention disorders, improve pronunciation, increase vocabulary, improve cognitive and memory functions, increase concentration of attention, reduce impulsive reactions in the form of hyperactivity and irritability;
- ensure pronounced positive dynamics in the form of normalization of the occipital  $\alpha$ -rhythm,  $\alpha$ -index and

spectral power, and normalization of its frequency, reduction of paroxysmal epileptiform discharges;

- a good safety profile manifested by good tolerability during the study was observed when using Anantavati® Kid.

Thus, the analysis of the data obtained after the use of Anantavati® Kids in children with perinatal CNS injury allows to suggest that Anantavati® Kids can be recommended for use in a comprehensive program of measures for the correction of cognitive, speech and sleep disorders, and impulse control disorder

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